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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,479	01/23/2004	Vivek Mittal	CSHL-P01-012	7041

28120 7590 01/24/2008

ROPES & GRAY LLP
PATENT DOCKETING 39/41
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
01/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/763,479	MITTAL ET AL.	
	Examiner	Art Unit	
	Maria B. Marvich, PhD	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2007*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,15-34,37,43-47,50-54,56-58,60,61,63-77 and 97-102* is/are pending in the application.

4a) Of the above claim(s) *7 and 75-77* is/are withdrawn from consideration.

5)☒ Claim(s) *6* is/are allowed.

6)☒ Claim(s) *1-4,8-12,15-22,25-34,37,43-47,50-52,56-58,60,61,63-74 and 97-102* is/are rejected.

7)☒ Claim(s) *5, 23 and 24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 November 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

The elected claims have not been found allowable and as such claims 75-77 remain withdrawn.

Drawings

Applicants' submission of black and white drawings is acknowledged. Applicants have stated that color drawings are not required of the invention and the publication of the black and white drawings will replace the color drawings previously filed.

Claim Objections

The previous objections to claims 1, 43, 44, 47, 60, 67 and 102 have been overcome by applicants' amendment. As regards claim 31, applicants argue that the recitation "by or to a binding site" Is intended to mean that the transcription factor can bind by the binding site or to the binding site. For clarity, it would be remedial to recite that --binding of the transcription factor to the recombinant RNA polymerase promoter is proximal to or at the binding site-- as the term "by or to a binding site" is grammatically inaccurate.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

Applicants' amendments have been persuasive in overcoming the rejections under 35 USC 112, second paragraph.

Claim Interpretation and Response to Amendment

The instant claims are drawn to a regulated polymerase III system comprising a recombinant polymerase III promoter that is regulated by a transcription factor whose expression is under control of an inducible promoter. During prosecution, claims must be interpreted as broadly as their terms reasonably allow. In the instant case, the term recombinant polymerase III promoter encompasses a variety of promoters whose relationship to pol III is not stated. Given the lack of structural requirements of the recombinant pol III, a broad interpretation of the claims *will include* an interpretation that the recombinant pol III promoter is any portion of the promoter in combination with any other promoter for example a TATA element. "While it is appropriate to use the specification to determine what applicant intends a term to mean, a positive limitation from the specification cannot be read into a claim that does not itself impose that limitation. A broad interpretation of a claim by USPTO personnel will reduce the possibility that the claim, when issued, will be interpreted more broadly than is justified or intended. An applicant can always amend a claim during prosecution to better reflect the intended scope of the claim." MPEP 2105.

Applicants argue that the claims should be read in light of the specification and as such the plain meaning of "pol III promoter" means that the promoter is one that can be used by RNA polymerase III. Applicants' arguments have been considered but are not persuasive for the following reasons. First, the specification does not explicitly limit the characteristics of a recombinant polymerase III promoter either functionally or structurally. Specifically, the specification does not define the term "recombinant polymerase III promoter" by a functional

transcription or that it can be used as a pol III promoter. Nor does the specification limit a recombinant polymerase III promoter structurally to a specific structure such as one that must comprise a PDS or a SNAPc. Application of Evans et al as art is based upon disclosure in the specification "In another embodiment of the regulated polymerase III expression systems described herein, the recombinant polymerase III promoter comprises a TATA Box. In a specific embodiment, the TATA Box comprises the sequence TATAAA. In some embodiments, the binding site for the transcription factor does not comprise a TATA Box, a mutant TATA box which differs by one nucleotide substitution from the sequence TATAAA, or a mutant TATA Box comprising the sequence GTATAAA". This passage teaches that a recombinant polymerase III promoter is distinguishable by its TATA box and Evans et al below meet this limitation.

Secondly, applicants argue that the tetO does not meet the limitations of a transcription factor, as it is not bound by a factor that increases expression but rather one that "represses". Claim 31 alones limits the activity of the transcription factor to be one that increases transcription from the recombinant RNA polymerase promoter. Absent the limitation in claim 31, claim 1 is open to interpretation that the transcription factor activates and represses expression. The promoter of Li et al is bound at the tet O site by tet repressor, transcription is blocked but removal of tet R results in procession of transcription.

Hence, the following art rejections stand.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 1, 2, 4, 8-12, 15-22, 25-33, 37, 43-45, 47, 50, 57, 58, 60, 61, 63-74, 97 and 99 stand rejected under 35 U.S.C. 102(b) as being anticipated by Evans et al (US 2002/0177564; see entire document).

Evans et al teach an RNA polymerase III promoter. Given the lack of structural requirements of the recombinant pol III, a broad interpretation of the claims will include an interpretation that the recombinant pol III promoter is any portion of the promoter in combination with any other promoter for example a TATA element as demonstrated in figure 2. The recombinant promoter is operable linked to at least 4 ecdysone response elements. Transcription factors that bind to these response elements are encoded by nucleic acid segments that express the factors under inducible promoter (see e.g. ¶ 147) as recited in claims 1, 2, 4, 11, 19, 30, 31, 33, 37, 60 and 99. The transcription factors comprise RXR and VgEcR (which alternatively can comprise a Gal4 domain) and are encoded by separate nucleic acid sequences and which encode DNA binding domains and transactivating domain (see e.g. figure 2). Expression by the transcription factor is dependent upon the presence of inducer (i.e. muristerone

or ecdysone) as recited in claim 12, 20, 21, 29, 63-74 and 97. Expression of the transcription factors (also known as regulatory proteins) is under control of an inducible promoter such as a tissue specific promoter and other promoters that are developmentally, temporally or cell cycle regulated (see e.g. 0170) as well as promoters that are regulated by inducers as encompassed by claims 15-18 and 28. The vectors comprising these constructs are used in mammals, which encompass cells and non-human organisms (see e.g. ¶ 28 and 43) as recited in claims 8-10. The regulated promoter further expresses a second "element" such as a sequence of a transgene or an enzyme or reporter genes such as luciferase that emit light or fluoresce, transcription factors and cell surface receptors (see e.g. ¶ 27, 36, 41 and figure 3) as recited in claims 43-45, 50 and 100. The vector for expression is pBluescript, which comprises restriction sites downstream of the pol II promoter as recited in claim 57 and 58. As recited in claims 26, 27 and 32 muristerone does not affect binding affinity of RXR to the promoter (see e.g. figure 2).

Claim 1-4, 8-11, 25, 28, 29, 30, 33, 34, 37, 43, 50-52, 56, 58, 60, 63-73, 98 and 99 stand rejected under 35 U.S.C. 102(e) as being anticipated by Li et al (US 2004/0146858; see entire document). **Claims 8 and 9 were indicated as rejected in the body of the rejection but were inadvertently left out of the heading in the previous rejection. Claims 8 and 9 have been added herein. However, upon reconsideration claim 53 has been added to the rejection as figure 6 teaches use of hairpin RNA. Hence, this rejection is a new rejection.**

Li et al teach an RNA polymerase III promoter (a mammalian U6 promoter) operably connected to a tetO site (see e.g. figure 3 and ¶ 120). Furthermore, a tet repressor is under expression of an inducible promoter (see e.g. ¶ 241-242) which inherently is activated in the

presence of an inducer as recited in claims 1-4, 11, 25, 28, 29, 30, 31, 33, 34, 37, 60, 63-73, 98 and 99. The vectors comprising these constructs are used therapeutically, which means that cells comprising the vector are found in the organisms that include as demonstrated in the examples, non human organisms as recited in claims 8-10. The recombinant pol III promoter is operably linked to siRNA as recited in claims 43, 50-52, 56. There are restriction sites downstream of the pol III promoter as illustrated in figure 1-2 and as recited in claim 58.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 46 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al (US 2002/0177564; see entire document) as applied to claim1, 2, 4, 8-12, 15-22, 25-33, 37, 43-45, 47, 50, 57, 58, 60, 61, 63-74, 97 and 99 above, and further in view of Cheng et al (Gene Therapy, 1997, Vol 4, 1013-1022; see entire document).

Applicants claim a regulated polymerase III expression system comprising a recombinant polymerase III promoter driving expression of a reporter such as GFP.

The teachings of Evans et al are described above and are applied as before except;

Evans et al do not teach use of GFP as a reporter.

Cheng et al teach use of GFP to assess gene transfer and expression in cells. Cheng et al teach that GFP is an important reporter molecule for non-invasively monitoring gene expression

and protein localization with in cells, the fluorescence does not require other co-factors and improved GFP molecules have been made such as S65T and RSGFP4 (See bridging paragraph, page 1013-1032).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the reporter as taught by Evans et al with the GFP as taught by Cheng et al because Evans et al teach that it is within the ordinary skill of the art to express reporter genes from a recombinant promoter and because Cheng et al teach that it is within the ordinary skill of the art to use GFP as a reporter. One would have been motivated to do so in order to receive the expected benefit that GFP is an important reporter molecule for non-invasively monitoring gene expression and protein localization with in cells, the fluorescence does not require other co-factors and improved GFP molecules have been made such as S65T and RSGFP4. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 54, 100, 101 and 102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al (US 2002/0177564; see entire document) as applied to claim1, 2, 4, 8-12, 15-22, 25-33, 37, 43-45, 47, 50, 57, 58, 60, 61, 63-74, 97 and 99 above, or Li et al (US 2004/0146858; see entire document) as applied to claim 1-4, 8-11, 25, 28, 29, 30, 33, 34, 37, 43, 50-52, 56, 58, 60, 63-73, 98 and 99 and further in view of Gardner et al (6,841,376; see entire document). **This is a new rejection.**

Applicants claim a regulated polymerase III expression system comprising a recombinant polymerase III promoter driving expression of ribozyme.

The teachings of Evans et al and Li et al are described above and are applied as before except;

Neither teaches an expression system used to express a ribozyme.

Gardner et al teach that existing expressions for use of regulating ribozymes production was available at the time of filing col 14, line 4-34). Gardner et al further propose an advance of these systems comprising a first nucleic acid sequence comprising an inducible promoter expressing a regulatory protein or transcription factor that regulates a promoter and a second nucleic acid that comprises a second regulatory protein or transcription factor that regulates expression from the first promoter (see e.g. figure 3b. There are at least two nucleic acid segments in the cell encoding regulatory proteins that bind to the regulated promoter as multiple nucleic acid segments are typically added to a cell for expression.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the reporter as taught by Evans et al with the GFP as taught by Cheng et al because Evans et al teach that it is within the ordinary skill of the art to express reporter genes from a recombinant promoter and because Cheng et al teach that it is within the ordinary skill of the art to use GFP as a reporter. One would have been motivated to do so in order to receive the expected benefit that GFP is an important reporter molecule for non-invasively monitoring gene expression and protein localization with in cells, the fluorescence does not require other co-factors and improved GFP molecules have been made such as S65T and RSGFP4. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent

evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

Claims 1-4, 8-12, 15-22, 25-34, 37, 43-47, 50-52, 56-58, 60, 61, 63-74 and 97-102 are rejected.

Claim 6 is allowable as the art does not teach a nucleic acid comprising SEQ ID NO:1.

Claims 5, 23 and 24 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Maria B Marvich, PhD
Examiner
Art Unit 1633